

Arena's investigational drug for insomnia may avoid side effects of market leaders, physicians say

Arena Pharmaceuticals' APD125 and other investigational sleep disorder drugs targeting the serotonin receptor could avoid the side effects seen in most of the approved insomnia medicines, doctors said. Arena's product appears to offer a far better side-effect profile than drugs that act on GABA-A receptors, which can lose their effectiveness over time, have the potential for abuse and dependency, and cause shallow breathing and next-day drowsiness known as a hangover effect. On the other hand, APD125 and others like it target the serotonin pathway, potentially avoiding problems seen with GABA-targeted drugs, the physicians said.

"This class of drugs seems to be more promising, because studies are showing that side effects are less with this drug," said Dr Carol Ash, medical director of Sleep for Life at the Somerset Medical Center in New Jersey.

For the estimated 30 million Americans with insomnia, there is not a large selection of treatments, Ash said. For example, she noted many over-the-counter treatments for sleeping problems contain benadryl, which can cause drowsiness. Prescription psychotropic drugs such as Valium and Xanax can cause more serious complications and lead to dependency. Although newer medications such as Ambien have a lower potential for abuse, they have a hangover effect, which can cloud decision making, she said.

The side effects associated with market-leading sleep drugs like Sanofi's Ambien, Sepracor's Lunesta and King Pharmaceutical's Sonata, which target the GABA-A receptor "might not occur [with serotonin-targeted drugs], considering it's a totally different pathway," said Dr Amit Verma, director of neurophysiology and sleep disorders at the Methodist Neurological Institute.

He also pointed to relatively new sleep drug, Takeda's Rozerem, which targets the melatonin receptor, as another beneficial step forward in treating insomnia.

APD125, which selectively targets the 5-HT_{2A} serotonin receptor to block a stimulatory pathway of the central nervous system, is in Phase II. Its maker, California-based Arena, recently completed enrollment in the randomized, double-blinded, placebo-controlled study, with 173 chronic insomniacs on board. The trial is evaluating the orally active compound's safety and efficacy with nighttime dosing.

The company is positioning it to help patients maintain their sleep.

Verma, who also is medical director of the sleep disorders center at The Methodist Hospital in Texas, said it remains too early to fully forecast APD125's future. But because it acts through a well-known pathway, he called it "a reasonable target to look at." He stopped short of saying that serotonin-targeted drugs would be the best option for everyone with sleep problems, noting that patient response would vary from one person to the next, given their different genetic susceptibility.

In the future, Verma predicted that drugs targeting serotonin could become part of the insomnia treatment standard, with drugs targeting GABA-A receptors also still part of the mix as they continue to get researched. Newer generation sleep drugs that target the GABA-A pathway are being developed to avoid side effects. Sanofi, maker of Ambien, is developing an insomnia drug that targets the serotonin pathway. Arena's market cap is about USD 734m and Sanofi's is USD 115.52bn.

by Aaron Lorenzo and Catherine Hollingsworth